

With the Author's kind regards

Hypodermic or Subcutaneous Medication.

With Special Remarks on Morphine, Atropine, Atropo-morphine,
and Apomorphine, and directions for making their
Hypodermic Solutions.

INTRODUCTION TO A DISCUSSION IN THE SECTION OF
PHARMACOLOGY AND THERAPEUTICS AT THE ANNUAL
MEETING OF THE BRITISH MEDICAL ASSOCIATION
IN CARDIFF.

BY

TALFOURD JONES, M.B.LOND.,

*University Medical Scholar; Fülliter Exhibitioner; Fellowes Medallist; Physician to
the Brecon County and Borough General Infirmary; Member of the Council
of the South Wales Branch; Vice-President of the Section.*

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WHEN I agreed to open the discussion on hypodermic medication in this Section, the Section of Pharmacology and Therapeutics of the British Medical Association, I did not then appreciate the difficulty of the task. The subject is one of vast extent, and one of daily increasing importance, and I shall find it no easy matter to say enough, and yet not weary you with too much. My thoughts, too, on this subject have been jotted down in the midst of the constant interruptions of a busy practice ; hence, I pray you to accord me your most patient indulgence.

It is to me an additional honour that I am privileged to address you in the presence of the two distinguished colleagues with whom I am in this Section associated.

Science is immensely indebted to Professor Fraser and to Dr. Murrell for innumerable physiological and therapeutical investigations ; and I trust they will pardon me if, in their presence, I remind you of a curious coincidence in their careers. Dr. Fraser obtained, in 1868, the Barbier Prize of the French Academy of Science, for his work on the *Physiological Action of the Calabar Bean* ; and Dr. Murrell has just been awarded the prize of the French Academy of Medicine for his investigations on nitro-glycerine.

It is now thirty years since Dr. Alexander Wood, of Edinburgh, in 1855, published his account of his method of introducing liquor morphicæ into the system by subcutaneous injection, and it is to him, undoubtedly, that mankind is indebted for the discovery of hypodermic medication. A few years later, in 1859, Mr. Charles Hunter published his important paper on the hypodermic treatment of disease. Since then, thanks to the labour of Lawson, Clifford Allbutt, Spender, and a host of others, the method has become widely known and practised. Dr. Wood advocated and practised the direct application of opiates to the painful points in neuralgic diseases. Hunter established the general fact that, for the relief of local pain, the injection of the remedial agent need not be made at or near the painful spot, but anywhere, at a distant part, provided it be fairly introduced beneath the cutis into the cellular tissue.

Dr. Henry Lawson, whilst believing in the general views of Hunter, was firmly convinced that, in most local neuralgicæ, a local injection answered best. Lawson was himself a martyr to sciatica, and was unable to move. He had tried nearly every remedy in vain ; at last, however, under advice, he was treated hypodermically with morphine, and with signal and immediate success, and in a few months he was restored to perfect health. He tried the effect of distant injections on himself, and on patients, in cases of sciatica ; and always with the same result, that there was far less immediate relief from pain. In brachialgia and lumbago, too, he was of opinion that local injections were best.

Anstie taught that Hunter's plan of injection at an indifferent spot was, in the great majority of instances, as effective as local injection ;

but, in instances of old-standing neuralgia, with development of tender points and centres of pain, it was advisable to inject at those points.

Rynd teaches that, in neuralgia, the nearer the injected fluid is brought to the uerves of the affected part, the better the result.

Von Graefe is especially careful to distinctly localise his injections.

Sommerbrodt has described a case of bilateral sciatica, in which the injection made on one side always resulted in the abatement of pain on the side of the injection, but not in the opposite limb.

Eulenburg has published a case of double sciatica, where the injection made at the painful spot always resulted in complete analgesia on that side, of two or three days' duration, whilst, on the other side, after the general narcotic effect had passed away, the pain immediately returned.

The evidence is such that it is almost impossible to deny that certain remedies do, when injected, produce, in addition to their general effect, a distinct local anæsthetic action. There are, however, some good authorities who still doubt the occurrence of any medicinal local action.

In my own practice, I have always proceeded in the belief that local neuralgiæ, and many local troubles, can be better treated by local injections. In lumbago and in sciatica I always inject, if possible, into the lumbar and gluteal regions; and in brachialgia, I have followed Lawson's plan of injecting the biceps, but I endeavour to avoid, if possible, the insertion of a needle into the face, the scalp, and the front of the neck, and my rule is only to inject at those sites when the local trouble is very severe, and of some standing.

You will see, if you look at the printed heading of this subject in our list of proceedings, that the term hypodermatic is used, and not hypodermic. Personally, I disclaim all responsibility for the use of this expression, and beg leave to shift it on to the shoulders of our two very excellent and energetic secretaries, though I have reason to think that Mr. Hancocke Wathen is the real culprit. But although I say this, I feel that Mr. Wathen, who is clearly a disciple of Bartholow, has acted wisely in thus giving us an opportunity of passing an opinion on it. Dr. Bartholow, of Philadelphia, in the last edition of his valuable work on *Hypodermic Medication*, has substituted hypodermatic for hypodermic; and philologically he is correct, and there are probably few, if any, scholars who would dispute it. The word is properly derived from the adjective *Δερματικός*, and not directly from *Δέρμα*. But even *Δέρμα* makes in the genitive *Δέρματος*, and it is clear that the stem is *Δέρματ*, and I am myself convinced that hypodermatic is correct. But if we give up hypodermic for philological reasons only, and substitute for it hypodermatic, we must also be prepared to substitute dermatic for dermic, endermatic for endermic, epidermatic for epidermic, and so on with numerous other adjectives, and, indeed, similarly with the adverbs of like origin; and we should therefore have to give up hypodermically, and say hypodermatically. But, to my mind, the old word hypodermic, like the corresponding term subcutaneous, is already too long a word, and if there be any change at all, I should prefer to see a shorter one employed. It has struck me that such a word as subdermal might be coined. It would be short and expressive. It might be objected that subdermal is a hybrid word; but so, too, is the common word suboxide, which is similarly made up of a Latin preposition and a Greek root. For the sake of brevity, I should prefer subdermal, and for a similar reason I hold that hypodermic is preferable to hypodermatic; but I do not advocate a change, for I doubt the wisdom of making an alteration now, and I am inclined to hope that you, too, out of respect to the memory of Charles Hunter, who introduced the word hypodermic, will think it well to avoid altering a phrase which has endured so long, and which is so universally accepted. And now let me return to more practical matters.

In subcutaneous injection, the fluid is rapidly absorbed by the lymph-vessels, the tissue-fluid canals, and the blood-vessels of the cellular tissue. Absorption is more rapid if the fluid directly enter open stomata of any of these canals. It is still more rapid if the fluid be accidentally injected into a vessel of perceptible calibre. Eulenberg uses the term intravenous infusion for those cases of intravascular injection in which the fluid is injected into a vein, and lymphatic infusion when it is thrown into a lymphatic. He has never seen a good example of the direct penetration of a subcutaneous vein of any calibre, and my own experience is similar, though I have seen several cases in which, judging from the rapid effects which followed, I believed that some minute vessels had been wounded; and in most of these cases I noted a drop or more of blood at the site of the puncture.

In Professor Hay's translation of Eulenberg's treatise on *Endermic and Hypodermic Medication*, which has just been published, he offers some important evidence on the quickness of elimination of drugs hypodermically injected. Thus administered, drugs pass more rapidly into the urine than after administration by mouth or rectum; their elimination begins sooner; their elimination also ends sooner, and the whole stay of the drug in the organism is shorter; and the inference is, that every single dose given hypodermically corresponds to a more intense, but yet a more evanescent, effect; and that a cumulative result is more difficult to obtain by subcutaneous injection from a succession of doses, than it is from administration by mouth.

Before proceeding further, I wish to offer some remarks upon hypodermic syringes, and then we will discuss the question of hypodermic remedies, and consider as many as time permits. The syringe which I use has been my pocket-companion for about eighteen years. I have used it thousands of times, and it is still in perfect working order. It was made by Weiss. The barrel is made of glass; the piston-rod and the fittings of silver. The piston-rod is graduated into half minims, and is furnished with a screw stopper, which can be twirled rapidly up and down the piston-rod, and which can be so fixed as to stop the movement of the piston at any required point. Many of the syringes now in use are based upon this principle; yet there are many practitioners who, possessing such a syringe, do not seem to appreciate the value of the stopper, and do not use it. When this is so, I have found that it is due either to a want of a clear perception of the proper way to use it, or to the fact, which is exceedingly common, that the piston-rod and the stopper are so badly made that the latter will not work properly on the former. It is essential that the stopper should be so adjusted that it can be made to run up and down the rod with the slightest touch or filip of the finger. When such is the case, no time is lost; indeed, time is saved.

I have dwelt on this point, because it is one which appears to me to be of much practical importance. Those only who are thoroughly conversant with its use can fully appreciate the many advantages of the stopper. With it, the injection can be introduced with greater rapidity, greater nicety, and greater accuracy. Twice in eighteen years it has been found necessary to put a fresh piston-leather to my syringe. On the last occasion, Messrs. Weiss fitted on one of their patent hard rubber pistons, which answers very well. I have not unfrequently seen a syringe brought out for immediate use in which the piston-leather, from its dry and loose state, rendered the syringe temporarily useless.

I have other syringes with plain leather pistons, that I keep for certain special purposes, which would, if not attended to, become invalidated. To obviate this tendency, we should examine all our syringes from time to time, and, if the piston-leather be dry and loose, all that is needed is to suck up some water into the syringe, and replace the syringe in its case. Allow me to add that our hypodermic syringes are not the only syringes that require to be kept in working order; and it will not uncommonly be found that the man who has a

hypodermic syringe that will not work has most likely an aspirator or an ear-syringe that will not act, and a stomach-pump that fails him when perhaps it is most urgently wanted.

The hypodermic syringe which I have described possesses nearly all the good qualities possible, and it is the type of syringe I advise all to possess. There are many similar ones now to be got, and some are graduated on the glass barrel as well as on the piston-rod, and this is an additional advantage. The syringe of Messrs. Burroughs and Wellcome is so graduated, and I find that the graduation of one that I possess is accurate on piston-rod and on barrel. Let me advise those who have not yet done so to examine and look for themselves into the graduation of their syringes, for in my experience the markings are more frequently wrong than right.

The hypodermic needle should be one that fits easily and yet firmly on the nozzle of the syringe, and it must not screw on. The screwing and unscrewing take up time, and there is no corresponding gain. The needle should be of the smallest calibre, and of the best steel. A steel needle penetrates more readily, with less force, and with less pain, and is less easily broken than gold or silver. For all general purposes, a short needle is best. It should measure about three-fourths of an inch, and should not exceed an inch. A short needle is less apt to break or bend, and it is easier to keep clean. For injecting deep tissues a second and longer needle is required, one about one inch and a quarter to one inch and a half in length. Instrument-makers have not paid sufficient attention to this matter. Those who supply hypodermic cases containing syringes, needles, and bottles, have overlooked an important point to which I desire to direct your attention. In all that are known to me, there is a want of due relationship between the length of the needle and the depth of the bottle. You see some cases with a long bottle and a short needle, others with a shallow bottle and a long needle. The needle, when affixed to the end of the syringe, ought to be shorter than the bottle which holds the remedy, so that it may be freely plunged to its full length without having its point injured by coming into contact with the bottom of the bottle; and yet it must be sufficiently long to reach nearly to the bottom, or it will not be able to suck up fluid when the bottle happens to contain very little of it. To meet this requirement, the needle should be one-eighth of an inch shorter than the bottle.

It occurred to me last month that I might design a hypodermic pocket-case, based on the principles I have just enunciated, that would be more generally useful than those at present in use. I wrote to Mr. Jahncke, of the Canonbury works, the maker of nickel plated bottle-cases, and sent him a plan of such a pocket-case, and he has successfully carried out my idea. He has taken pains to obtain a reliable syringe, and proper needles and bottles, and I trust he will be compensated and rewarded for the trouble he has taken in following my directions. The case is a shallow one, and measures only four inches by one inch and seven-eighths, and contains a syringe, two needles, and five bottles. Two of the bottles, which are larger than the remaining three, are intended for the solutions most commonly used, namely, morphine, and mixed morphine and atropine; the others will do for, *e.g.*, atropine, apomorphine, and pilocarpine. Another and similar case is fitted up with bottles only, seven in number, and this I have dubbed a "supplementary hypodermic case." It is intended to hold those hypodermic remedies that are not wanted every day. Any one who possesses both cases will have bottles for twelve different medicines. The hypodermic case is intended to be a pocket-companion; the supplementary one is also intended for the pocket, but usually it will be kept in the doctor's bag; but since the bottles are alike in each it will be easy to take, for any special use, a bottle out of the supplementary case, and put it into the one containing the syringe. I may mention that the cases will exactly accommodate the bottles

in which Messrs. Burroughs and Welleome send out their hypodermic tabloids.

Before concluding my remarks on syringes, allow me to call your attention to the useful hypodermic injector of our most inventive associate, Dr. Ward Cousins. It consists of an elastic measuring ball and an injecting syringe. Balls are made in various sizes, each ball holding only one definite quantity of fluid. It is safe, cheap, and handy, and is the only syringe that ought ever to be left in inexperienced hands.

Let me now direct your attention to the solutions used for hypodermic purposes. A typical solution should be absolutely pure, as nearly neutral in reaction as possible, free from solid particles and fungoid growths, and not too concentrated.

Bartholow states that the most carefully prepared solution rapidly deteriorates by keeping, and that, although antiseptics may be useful in preserving them for awhile, he thinks it far better to make extemporaneous solutions. I acknowledge that weak solutions of most alkaloids soon undergo a change, and become cloudy or turbid from the growth of mould-fungus; but this, according to my experience, is not the rule with strong solutions. In many instances, alkaloids are themselves destructive to such low forms of life as bacteria, vibrios, and mould-fungi; and I find this to hold good with a strong solution of morphine, or a strong solution of mixed morphine and atropine, the very two solutions above all others that we most frequently use. There are many authorities now-a-days who seem to think it quite impossible to keep a so-called permanent solution for any reasonable time, unless it be mixed with an antiseptic.

By a permanent solution, I simply mean a ready-made solution that will keep from a few weeks to a few months; and, by an extemporaneous solution, one that can be made by dissolving the remedy in water at the bedside of the patient. For the latter purpose, Messrs. Burroughs and Welleome make small tabloids which contain a definite and reliable dose of the remedy, which keep well, and are readily and entirely soluble in water. They are much superior to the old gelatine-discs, and, for extemporaneous purposes, I know nothing better. But it is indisputable that reliable permanent solutions are preferable, in most cases, for reasons which it is quite unnecessary to discuss.

Morphine.—Let us proceed to inquire into the question of permanent morphine-solutions; but, before I forget, let me bear testimony to the very valuable standard solutions of Messrs. Allen and Hanburys. They are uniform and permanent, and they have the special feature of being made to a standard dose. The ordinary dose of each solution is five minims. This is undoubtedly an advantage, and especially for those who do not often use hypodermic remedies, and cannot bear in mind the different doses. The solutions that I have tried act well, and much wisdom has been shown in fixing upon the dosage, with the exception of the morphine-salt, which, at a quarter of a grain, is fixed, as I shall attempt to show presently, too high. Mr. Martindale's solutions have been longer known, and are always reliable.

Of permanent solutions, the first that claims our attention is that of morphine. The injectio morphinæ hypodermica *P.B.* contains, or is supposed to contain, 1 grain of acetate of morphine in 12 minims. The process of making it is tedious, and the result is somewhat uncertain. Various statements have been made, not only about this solution, but also about differently made solutions of the acetate. Many speak well of it; others say it is liable to change after a very short time, that fungoid growths soon appear, that the solution quickly becomes turbid, that it throws down much deposit and becomes weaker, that it becomes very brown, that it is irritating to the tissues, and that it is often followed by sores and indurations, that the needle becomes clogged, and that for these reasons many prefer to use the

neutral tartrate or the bimeconate, and some prefer the sulphate, but still more, I fancy, use the hydrochlorate.

My own experience of the acetate is quite the reverse of all this; but then it is only right to add that I have never used the pharmacopœial preparation, nor have I ever used an acetate of morphine solution that has not been made by myself; and I would strongly advise all those who practise hypodermic medication to make for themselves as many as possible of the solutions they use.

Of all the salts of morphine, there is not one, in my opinion, equal to the pure and freshly made acetate. The acetate contains 10 per cent. more morphine than the sulphate, and 6 per cent. more than the hydrochlorate, and I will endeavour to prove to you that it is the best salt of morphine for making a hypodermic solution. For twenty years, I have used no other form of morphine-solution than the acetate, and I have never had occasion to be dissatisfied with it.

With your permission, I will relate my own experience of this solution, and explain my method of making it. For about sixteen years, I have invariably made it in one and the same way, and of the same strength. I believe I was a good deal influenced by Anstie, whom I admired and respected, in fixing upon the strength and upon the form of the solution itself. The strength is the same as that adopted some years after by the Pharmacopœia Committee, namely, 1 in 12.

The acetate of morphine to be used for making a solution must be pure and fresh; the fresher the better. To make an ounce of the solution, proceed as follows: procure a stoppered bottle that holds exactly one fluid ounce; half fill this with water, which I never use distilled; then put into the bottle 40 grains of acetate of morphine, and drop into it exactly 4 minims of acetic acid (*B.P.*) Shake, and the salt will instantly dissolve; then fill the bottle with water. The resulting solution will be pale and clear. Such a solution, if properly kept, will not in six months throw down more than a fraction of a grain of the acetate. It will perhaps become darker in colour, but this is immaterial. It should be kept in a cupboard or in a case, away from the light; and this bottle should be treated as a stock-bottle, and should not be opened except for the purpose of supplying the smaller bottle of the hypodermic case.

It may be as well to point out, for the sake of those who use very little morphine, how to make a small quantity, say a fluid drachm. Take a drachm bottle, and use five grains of the morphine salt, and half a minim of acetic acid, and fill as before with water. If a dropping pipette be used, it will be easy to deliver half a minim, which is represented by one ordinary drop from the point of a medium-sized pipette; or if this be not at hand, it may, perhaps, be easier to measure out four minims of the dilute acetic acid (*P.B.*), which exactly represents half a minim of the strong acid. No more acetic acid should be used than is required to make the solution perfectly clear. The injection thus made contains only a fraction more than eight minims of acetic acid in 1,000 of the solution. A fluid ounce of this injection can be made for eightpence, that is, a penny a drachm, and each drachm will suffice for twenty quarter-grain injections; yet a very well-known London chemist the other day charged no less a sum than twenty-five shillings for a single ounce of a morphine solution. In making my solution, I have invariably used a morphine acetate prepared by the eminent chemists, Messrs. Battley and Watts. I have brought with me for your inspection, a few solutions made exactly in the way described. I regret that I have not a specimen of one older than six or seven months. Here is one that was made in January this year. I examined it on June 28th, and found that it was perfectly clear, of a pale sherry brown colour, with only a small fraction of a grain of deposit, partly amorphous, but chiefly crystalline, and no trace of mould-fungus. Here is another solution made on June 26th from a morphine salt some months old; and one made on July 6th, from a perfectly fresh salt. You will perceive that the last one is very free from colour.

Here is a specimen of the Pharmacopœia injection which was given me by a friend, and which looks ill indeed by the side of my solutions. But I have this week seen in a chemist's shop a good specimen of the British Pharmacopœia solution, about three years old, clear, of a brown sherry tint, and with only a trace of deposit.

In spite of the introduction of many new remedies, morphine is still the most generally useful of our hypodermic agents. It is only eighty-one years since this, the first known alkaloid, was discovered. Since then, our knowledge of active principles has been ever increasing. New natural alkaloids are constantly being added to our list, and chemists have already made some of them synthetically, and will, probably, soon find out the way to make most of them by artificial means.

The number of active principles which can be utilised for hypodermic purposes is, consequently, increasing, and the practice of hypodermic medication is, in this sense, becoming more difficult; and it requires from the practitioner a deeper and a more precise knowledge of physiology, pharmacology, and therapeutics.

One of the most important points we can consider is that of dosage, and especially the dosage of morphine injections. A moderate dose of morphine is soon followed by a feeling of rest, contentment, and well being, and pain will be lulled or abolished, and later on this condition will in most instances be succeeded by drowsiness or sleep. But, if the dose be large, deep coma may occur almost immediately, without any preliminary stage. It should be our aim so to apportion the dose, that this too rapid onset of narcosis may be prevented. We should be doing good service if we could, in this Section, agree upon a fairly wide and yet a safe dosage for hypodermic morphine, and, if time permit, the dosage also of the more important of our other subcutaneous remedies. Lawson's advice was not to begin with a larger dose than one-sixth of a grain. In three of his cases, the largest dose that could be given without exciting vomiting was one-twenty-fourth of a grain. Austie used to say, never commence with a larger dose than one-sixth of a grain; often one-twelfth of a grain will give effective relief. With one-sixth of a grain, as a rule, no distinct narcotic effects are observed, no contraction of the pupil, no heavy stupor; and, though the patient falls asleep, on awaking he has no headache, or furred tongue. Dr. H. C. Wood says, "I have seen alarming results from the injection of one-sixth of a grain, and half a grain has produced death." He advises that in females, unless very robust, the maximum dose should be one-eighth of a grain; in men, one-sixth to one-fourth of a grain. Ringer says, "A larger quantity than one-sixth of a grain sometimes produces serious consequences."

I remember, when first reading, in 1874, Dr. Spender's Fothergillian prize essay on the relief of pain, noting with satisfaction his wise remarks on the necessity of great caution in administering hypodermic morphine. I will quote his own words. "Even by esteemed authorities the initial dose of morphia under the skin is announced too high; it is prudent for this never to exceed one-tenth of a grain for an adult female, and one-eighth of a grain for an adult male." A few weeks before reading this, I had myself witnessed most alarming symptoms from an injection which I had administered to a lady. She was a thin delicate woman, suffering from severe facial neuralgia. I very carefully measured out one-twelfth of a grain of morphine, and injected it into her arm; and with complete relief to her pain, but, with such general ill results, that I was unable to leave her for many hours, and was obliged to administer frequent doses of strong coffee and ammonia. This lady had informed me that she was very susceptible to the action of opium, but I then thought that one-twelfth of a grain of morphine could not possibly hurt her. Afterwards I felt thankful that I had been so far cautious about the dose. Please note that this lady was rather small in build, and light in body-weight. This reminds me, that I should not forget, whilst discussing this question of dosage,

that it is of vital importance that we should bear in mind that, other things being equal, the dose of a drug must be apportioned according to the body-weight of the patient; due allowance being made, of course, for much fatty tissue.

I have never administered morphine hypodermically to young children. It ought, if possible, to be avoided. It can rarely be found indispensable; and, under the age of 5 or 6 years, other means should be employed. If ever used, we should bear in mind the relatively larger brains of children, and, after having made due allowance for body-weight, give no more than half the otherwise proportional dose. It is scarcely necessary to allude to other conditions affecting the dosage of morphine, for in other respects we should be guided by the rules that apply to the administration of morphine by the mouth.

Properly, we ought, in considering this question of morphine-dosage, to be guided by our official pharmacopœia. In the *British Pharmacopœia*, the dose of the morphine-salts is fixed at one-eighth to half a grain; but the dose of the morphine-solutions which are made from these salts is fixed at ten to sixty minims—that is, one-twelfth of a grain to half a grain. I regret to add that this want of uniformity between the doses of these salts and their corresponding solutions is only one of many similar errors which may be found in our official guide.

Given by the mouth, several instances are recorded in which one grain of hydrochlorate of morphine has caused death in adults. The half-grain maximum dose, therefore, of the *Pharmacopœia*, for ordinary internal administration, may be put down as corresponding to half a lethal dose. Now, what is the pharmacopœial dose for hypodermic morphine? It is fixed, most strange to say, at one-twelfth to half a grain, which is precisely the dose laid down for administration by mouth. What do we learn from looking over the records of death from the hypodermic administration of morphine? We find that numerous cases have been recorded, in which half a grain of hypodermic morphine has caused death in adults. Cases have been reported in the first volume of the *Medico-Chirurgical Transactions*, and in the *Medical Times and Gazette* for 1868, in which a quarter of a grain or a somewhat greater quantity of subcutaneous morphine has been followed by syncope, with struggling for breath, and apparent imminent or even present death. I am myself aware of a case in which death was caused in a male adult, by a dose stated by the operator to have been only a fourth of a grain. From inquiries I have instituted, cases have been brought to my knowledge in which half, one-third, and even one-sixth of a grain of morphine has caused death. The half-grain maximum dose of the *Pharmacopœia* is, therefore, without a doubt, a lethal dose for many adults. Authorities agree that morphine injected subcutaneously is at least twice as potent as morphine given by the mouth; but evidently the framers of the *Pharmacopœia* were either not alive to this, or did not believe it.

Unluckily, most chemists label their morphine-solutions with a dose based upon the pharmacopœial authority; and many persons have been led astray, and have given dangerous and fatal doses. For most of this, for many accidents, and, I fear, for many deaths, we have to thank the *British Pharmacopœia*. We can come, I think, to no other conclusion than that the official dose of hypodermic morphine ought to be reduced to one-half, and, which comes to the same thing, should be definitely fixed at half that now authorised for administration by mouth; and the dose then would be from one-twenty-fourth to one-fourth of a grain. This would be a safe guide for the inexperienced; it would especially assist in making men cautious about their first or initial doses. Those who care to exceed a quarter of a grain must do so on their own responsibility. We know, of course, that in many cases of extremely acute pain, and in many painful chronic diseases, it is absolutely necessary to push morphia to the extent of half a grain or more. The practitioner must, in such cases, judge for himself;

but, for all first or initial doses, it would be well to make it a rule never to exceed one-eighth of a grain for an adult female, and one-sixth of a grain for an adult male.

Atropine is the remedy that I rank next in importance to morphine. A hypodermic solution of atropine is one of the easiest possible to make. The sulphate is the best salt to use. Martindale, who is a good authority, recommends the crystalline sulphate. I have always used the amorphous salt of the *Pharmacopœia*. For fifteen years, I have used a two-grain-to-the-ounce solution, and I have found it a very convenient strength. It is exactly half the strength of the liquor atropiæ sulphatis of the *British Pharmacopœia*, and can be made by simply mixing equal quantities of that solution and water.

But, in order to have a really fresh solution, proceed as follows. Put into an ounce stoppered bottle two grains of the sulphate, and fill the bottle with water. The salt will instantly dissolve, and the solution is made. If chloroform-water or camphor-water be substituted for plain water, the solution will keep a little better. This injection contains one grain in four drachms, or in 240 minims; therefore

1 minim contains	$2\frac{1}{40}$ grain
2 minims contain	$1\frac{1}{20}$ "
3 " "	$\frac{3}{20}$ "
4 " "	$\frac{1}{5}$ "
5 " "	$\frac{3}{40}$ "
6 " "	$\frac{1}{10}$ "

This is also a convenient strength for ophthalmic purposes. The hypodermic dose that I can recommend is from $2\frac{1}{40}$ th to $\frac{1}{40}$ th of a grain; that is, from one to six minims. A fair initial dose is $\frac{1}{20}$ th of a grain. Beyond $\frac{1}{40}$ th of a grain, the remedy, if used at all, must be used with increasing caution and watchfulness. In some people, atropism is induced by doses of even $\frac{1}{40}$ th of a grain.

I think I have noticed that those who are most susceptible to atropine are the least influenced by morphine, and *vice versa*. This is certainly so in children. Patients are very apt to be frightened when, after an injection of atropine, the physiological effects are at all marked, and the practitioner himself may become needlessly alarmed. *Apropos* of this, let me quote an aphorism of Bartholow, that "severe physiological effects do not necessarily imply a condition in which life is endangered." The maximum fatal dose of atropine is unknown to me. The dose has often been pushed to one-twelfth or to one-tenth of a grain, but one-twentieth of a grain or less has been known to produce alarming symptoms. I have only once given as much as one-thirtieth of a grain, and the case in which it was used was alluded to by me in a paper on nitrite of amyl, which appeared in the *Practitioner* in 1871. It was the case of a man who suffered severe colicky pains due to fecal accumulation, and one injection of one-thirtieth of a grain of atropine relieved the muscular spasms, and caused within an hour a free action of the bowels. This dose produced very distinct, but no ill, symptoms. We cannot discuss the uses of atropine without glancing, however briefly, at its physiological action. Small doses do not appear to affect the respiration, whereas full medicinal doses accelerate it; and very large doses stimulate, and then paralyse, the respiratory centre. With regard to this point, we have chiefly to bear in mind that it is a respiratory stimulant, and that full medicinal doses strengthen and quicken the respiration. On the circulation, it also produces varying effects, according to the dose; but again we must chiefly bear in mind that it is a cardiac stimulant, and that in full medicinal doses it causes increased rapidity and force of the circulation. On the sensory nerves, it induces lessened sensibility, and on involuntary muscular fibre it causes varying states, according to the dose.

It will be sufficient for our purpose if I give you a slightly con-

densed summary of Brunton's views of its action on the intestines. He says: 1. Small doses increase peristaltic movements. 2. Moderate doses arrest them, but the muscular fibres of the intestine retain their irritability. 3. Large doses stop peristalsis, and also paralyse the muscular fibres of the intestine.

Again, I would have you chiefly to bear in mind that, on unstriated muscular fibre, medicinal doses cause relaxation and muscular quietness, and full doses paralysis. Atropine also checks the secretions of the salivary and sweat-glands, and the secretions of most other glands. It is well to note that atropine is very rapidly eliminated from the system, and chiefly by the urine.

Let us, now, consider the medicinal uses of atropine, under four headings.

1. *As an Anodyne and Antispasmodic.*—Its action on sensory nerve-endings and on involuntary muscular fibre teaches us that it possesses anodyne and antispasmodic qualities. Anstie held that belladonna was the best medicine for every kind of pain in the pelvic viscera. He believed it was far inferior to morphia as a speedy and reliable reliever of neuralgic pain, but, for all forms of pelvic neuralgia, it surpassed morphia.

As a general pain-reliever, no one would think of comparing atropine with morphia; but, in certain painful conditions, its value is beyond question. The chief indication for its hypodermic use is painful muscular spasm; and, for this purpose, a local injection is better than a distant one. It has been found useful in painful spasms of the intestines, bladder, uterus, urethra, and bile-ducts. Hence its value in spasmodic intestinal colic; in the passage of gall-stones, or renal calculi; and in laryngismus stridulus and spasmodic asthma.

2. *As an Anhydrotic or Sweat-lessener.*—Here its use is indisputable. The general hyperidrosis occurring in phthisis, in debility, or in women during the climacteric, is always much relieved by atropine. An injection of $\frac{1}{160}$ th of a grain, or sometimes $\frac{1}{40}$ th of a grain, will stop the sweating, and put the patient into a comfortable state. It is similarly useful in salivation, and as a local injection in a painfully distended or inflamed mamma.

3. *As a Respiratory and Cardiac Stimulant.*—It is useful in depressed or paralysed conditions of the centres, regulating the breathing and circulation; and it has been thus used with advantage in pulmonary congestions, and to counteract heart-failure in syncope, in shock, and in typhus fever. But these stimulating properties are best considered under a fourth heading.

4. *As an Antidote.*—It is here that we see its astonishing value, when subcutaneously employed. In the February number of the *Practitioner* for 1870, Professor Fraser, in discussing atropine as an antidote to physostigma, made the following remark. He said that "no investigation could possibly be undertaken that would more certainly advance the science of therapeutics, increase its resources, and remove irrational scepticism, than that of the antagonism of remedies." I am a firm believer in the soundness and the wisdom of this opinion. It has been demonstrated by our President that, within certain limits, a very marked antagonism exists between atropine and eserine.

Atropine is also antagonistic to morphine and opium, muscarine and poisonous mushrooms, aconite, pilocarpine, chloral-hydrate, quinine, gelsemine, and nitro-glycerine, and perhaps to prussic acid; but this does not exhaust the list. Bartholow says it is antagonistic to tartar emetic and veratrine.

Atropine, as a respiratory stimulant, is especially useful as an antidote to morphine or opium; but it is also well to bear in mind its additional value as a cardiac stimulant, for, as mentioned by Ringer, patients may die after opium, in a state of collapse, and not from asphyxia, though death, as we know, usually happens from paralysis of respiration.

But death, too, may occur after morphine from syncope. To avoid

the chance of such an occurrence, it is well always to give the injection in the lying or sitting posture, and, if possible, in the former. In all susceptible or weak people, and in women especially, the patient should always be made to lie down, and should be kept in the recumbent posture, and under observation for at least ten minutes; and ammonia, nitrite of amyl, and atropine should always be at hand.

I will conclude the subject of atropine by giving you some brief details of a case in which it was necessary to inject atropine to counteract the effects of pilocarpine; and they will, to a certain extent, serve to illustrate Dr. Fraser's aphorism which I quoted just now. Three years ago, I had occasion to use a hypodermic injection of pilocarpine, in a woman, a chronic sufferer from asthma. She had tried almost every remedy, and was willing to submit to any treatment. I explained that she would perspire profusely, would perhaps secrete a lot of spittle, and would probably bring up mucus from her chest, and that in this way she might expect to get some benefit; and she was informed that, if she should feel exhausted by it, these effects could be stopped in a few minutes by the help of another and counteracting remedy.

I injected one-sixth grain of hydrochlorate of pilocarpine, which quickly caused intense perspiration; saliva soon began to trickle from her mouth; her sight became so dim that she could not distinguish anything, yet her pupils were scarcely at all contracted. In a quarter of an hour, retching set in, and some bronchial mucus, but not much, was expectorated; then vomiting occurred. Her pulse became very feeble, and, though feeling hot, she shivered. At the end of thirty minutes, she was so exhausted and pale, and so inclined to faint, that I felt somewhat anxious, and immediately injected $\frac{1}{100}$ th of a grain of atropine. At that time she was sweating profusely. In five minutes the perspiration had nearly ceased, her pulse rallied, and she began to feel easy; and, in another few minutes, the skin was quite dry, and she was feeling quite herself, and much relieved in her breathing.

This patient was so much benefited by the pilocarpine that, in some subsequent asthmatic attacks, she begged for a repetition, saying: "It made me feel very distressed and faint, but the other medicine put me all right." On these other occasions I used a smaller dose, one-eighth of a grain, and this acted sufficiently well, and no atropine was needed.

I have no personal experience of the hypodermic use of those other alkaloids that much resemble atropine. Duboisine is stated by Eulenburg to be twice as strong as atropine. Daturine is probably a mixed alkaloid. Hyoscyamine can be given in the same dose as atropine. Homatropine is given in smaller hypodermic doses, though its local ophthalmic effects are milder and of shorter duration than those of atropine. I have by me a solution of the hydrobromate of homatropine, four grains to the ounce, made by Corbyn more than two years ago, which is now perfectly clear and pure.

Morphine and Atropine combined.—Having discussed morphine and atropine separately, we have now paved the way for the consideration of the conjoint use of morphine and atropine. We have not, to my knowledge, any name for mixed morphine and atropine, and it has just occurred to me that we might call it atropo-morphine. Atromorphine would do, and is shorter, but it is not so expressive, and it is, too, like in appearance and in sound to apomorphine. If we use atropo-morphine, we must pronounce the *o* short, as in the Greek. It was about twelve or thirteen years ago that I began to use atropo-morphine, and I soon decided to employ a solution that would correspond to my morphine and atropine ones; and ever since I have used no other.

This atropo-morphine solution is made by simply adding two grains of sulphate of atropine to an ounce of the hypodermic solution of the *British Pharmacopœia*, or to an ounce of my morphine-solution already described. We thus get a solution that contains one grain of morphine and one-twentieth of a grain of atropine in twelve minims.

Those who care to adopt the three different solutions of morphine,

of atropine, and of atropo-morphine, which have now been described, and which I have found generally convenient and suitable, will possess in three bottles two solutions of morphine and two of atropine, and in each couple the morphine and the atropine will be of the same strength, and it is, therefore, easy to remember the quantity of alkaloïds in them; for it is only necessary to bear in mind the strength of the atropo-morphine solution, namely, that one minim contains one-twelfth of a grain of morphine, and $\frac{1}{240}$ th of a grain of atropine. This mixed solution, you will note, contains morphine and atropine in the ratio of twenty to one; and some good observers quote this proportion as being the proper one for bringing out the best conjoint results of atropo-morphine.

It may not be inappropriate here to state that for many years I have also used this same proportion in all my atropo-morphine suppositories; and one of the most generally useful suppositories I know is made for me by Messrs. Battley, with one-quarter grain of acetate of morphine and one-eightieth of a grain of sulphate of atropine, namely, twenty to one. The atropo-morphine solution keeps very well. Here is one made in February of this year: I examined on June 28th the stock-bottle from which it was taken. It was clear, of a pale sherry colour; and, just as in the accompanying morphine-solution, there was a fraction of a grain of amorphous and crystalline deposit; no trace of mould-fungus. The solution is now clear and pure.

Let us now consider the conditions that indicate the use of atropo-morphine in preference to morphine.

The conclusions at which I have arrived are these.

1. Fairly small and moderate doses of atropine slightly increase the hypnotic properties of morphine. This is a matter of doubt with many; some deny that atropine does this, while others even say it very decidedly lessens the hypnotic action.

2. Atropine in medicinal doses increases the anodyne properties of morphine, and this increased anodynia is more marked in local than in distant injections.

3. Atropine in moderate doses counteracts the depressive action of morphine on the heart, and lessens the tendency to sickness, giddiness, and faintness; and, by its influence on the circulation and on the skin, it also tends to prevent the clammy sweat, the pallor, and the coldness that morphine not unfrequently induces.

4. In small doses it does not influence, to any appreciable degree, the action of morphine on the respiration; but when given in fair medicinal doses, and, *a fortiori*, in larger doses, it increases the number of respirations per minute, and augments their depth.

We may now apply the preceding conclusions to practical medicine. In a weak, a fatty, or a dilated heart, we incur the risk of inducing a syncopal state by hypodermic morphine; hence it must be used with extreme caution in such conditions, and it is safer to make it a rule to use not morphine alone, but atropo-morphine in such cases. Of course, there are many cardiac troubles and forms of cardiac dyspnoea in which morphine can be used alone with infinite benefit; and this was pointed out long ago by Allbutt and Ringer; but in the preceding states alluded to, and especially in women, it is better to use atropo-morphine. In hepatic, renal, and intestinal colic, in spasmodic asthma, and in ovarian and uterine neuralgia, and in the painful spasms of tenesmus, atropo-morphine is better than morphine; and similarly, in all these conditions, but especially in the last three, atropo-morphine suppositories are much better than those of morphine.

In most neuralgiæ, and especially in ophthalmic neuralgia, atropo-morphine is the better remedy.

In sciatica, lumbago, brachialgia, and in most forms of myalgia, and in cramp of muscles of the limbs, atropo-morphine is preferable to morphine.

In muscular cramps, I have obtained better results when the atropine has been used in greater relative strength than one in twenty.

For that peculiar condition of breathing called "Cheyno-Stokes," I have found atropine alone decidedly useful; and if morphine for any reason be needed in such a condition, it should be combined with a preponderating dose of atropine.

I find that, during recent years, I have been using atropo-morphino more and more, and I now use it more frequently than morphine, and I rarely use atropine by itself.

The mixed solution already described answers very well for most purposes, but when the dose in chronic cases, or by reason of habit, has to be increased beyond six minims, the corresponding dose of atropine has occasionally to be diminished. Conversely, there are some so very susceptible to small doses of morphine, that they need a proportionately larger dose of accompanying atropine.

It is easy, having the three different solutions in one case, to adjust for any special occasion any combinative dose of the alkaloids that may be deemed desirable.

I will now ask your attention to a class of troubles in which I hold that it is advisable to give morphine without atropine, or, if the latter be combined with morphine, the morphine must be in sufficient excess to exert a preponderating influence over the atropine.

This class of painful troubles includes pleurisy, fractured ribs, and wounds of the chest-walls, abscess of the thoracic walls, cancerous infiltration of the chest-wall, pleurodynia (that is, thoracic myalgia) and intercostal neuralgia. In all these cases, though only in a slight degree, perhaps, in intercostal neuralgia, we wish to lessen or modify the chest-movements, both those of expansion and elevation; we wish to prevent, as much as possible, the stretching of the intercostal muscles and of the pleura; and, in those conditions, patients make voluntary efforts to restrain the breathing. In adult females, this need is all the more felt, because their respirations are chiefly thoracic.

Let us take pleurisy as the most common member of this class. We know that the pain of the early stages of acute pleurisy is intensified by respiration, and is often rendered agonising by a deep breath or a cough. What is the treatment?

I will mention two proceedings that are almost indispensable if we desire to give the maximum of relief. The first thing to do is to give, as quickly as possible, some hypodermic morphine; and the next is to bandage, or rather strap, the chest-wall after the fashion suggested by my friend, Dr. Frederick Roberts. The morphine will ease the pain and quiet the breathing, and the plaster will lessen the movements of the thoracic walls. It is in this class of cases that I have found it better to give morphine alone, or morphine with a minimum quantity of atropine.

If atropine be allowed in these cases to exert a preponderating influence, its stimulating effect on the heart and lungs is decidedly prejudicial. Again, in painful affections of the diaphragm, the more rest we can secure for it the better. For this reason, phrenic or diaphragmatic pleurisy may be included in the preceding class. The paroxysmal dyspnoea, and the agonising pain of a deep inspiration in this affection, can best be treated by morphine alone.

Peritonitis is another disease that ought to be, and indeed generally is, treated on similar principles. The patient assumes naturally a position best suited to relieve abdominal tension, and tries to restrain abdominal respiration by exerting his influence to lessen the depressive movements of the diaphragm. In this disease, atropine is contra-indicated. The respirations are already too hurried, and the heart's action too rapid. The one remedy is opium, which is best given in the form of hypodermic morphine.

Apomorphine.—An important derivative of morphine next deserves our attention. Hydrochlorate of apomorphine is not yet as widely known and appreciated as its merits deserve. It stimulates the vomiting centre

of the medulla oblongata, and acts as a rapid, certain, and safe emetic. It has been used hypodermically to produce emesis in cases of poisoning, alcoholic intoxication, and the like. A fellow student of mine, Dr. Samuel Gee, was the first to announce its prompt emetic action, and he gave it in doses of one-tenth of a grain hypodermically.

Other and later observers found that one fifteenth of a grain sufficed in almost all cases to induce vomiting in five to ten or twelve minutes. One-tenth of a grain usually causes vomiting in three to five minutes. Until the last year, this is the dose I have usually administered to adults; but now I use a smaller one, and find that one-twentieth of a grain suffices to cause a sufficiently speedy, and a less prolonged emesis. A common strength is a 1 in 50 solution, but a still better for a permanent solution is 1 in 100, or 1 in 120. One advantage of this weakened preparation is, that a definite dose for administration by the mouth can be more easily measured out and used out of the same bottle for children. I would suggest the following dosage for hypodermic apomorphine; for adults, one twenty-fifth to one-tenth of a grain; that is, four to ten minims of a one per cent. solution. In a few very exceptional cases, sudden collapse has occurred after one-twentieth of a grain. Still, no one need have the slightest hesitation in injecting one-twentieth of a grain into an average sized adult, whenever the symptoms warrant its use, and, if need be, the dose must be repeated. Of course there are cases in which a larger dose can be, and ought to be, administered at once. For children, a fourth of the adult dose may be used, that is, one-hundredth to one-fortieth of a grain, that is, one to two and a half minims of the one per cent. solution, more or less according to the body weight. But, except in cases of urgent necessity, it is better not to use it hypodermically in children. I will quote two cases illustrative of its use.

D. E. was suffering from a severe and prolonged epileptic attack. On two former occasions I had roused him out of his fits by nitrite of amyl, but amyl failed now. His friends were very uneasy, and finding, at the end of an hour, that he was no better, I gave him a hypodermic injection of one-tenth of a grain of apomorphine. In three minutes vomiting set in, and he then became conscious, and had no relapse. In this instance the vomiting lasted off and on for half an hour; he was then put to bed, and went to sleep, and awoke in the morning fit for work. Last month, I saw a man in a state of hysterio-epilepsy. He had been drinking freely of beer. Fits began at 9 P.M. I was sent for some time after midnight. The face was not flushed. Several men were heading him down. He kept putting out his tongue to its full length towards the right side, and then withdrawing it, repeating this movement every three or four seconds. He never bit it. Hypodermic injection of one-twentieth of a grain of apomorphine caused vomiting in four to five minutes; a quart or more of beery fluid came up, and he at once answered questions. The vomiting was all over in fifteen to eighteen minutes, and then he went to sleep, and awoke quite well.

Apomorphine is very soluble in water, but after a time an aqueous solution changes to a deep green colour. Last year I had occasion to use, in the absence of a fresher solution, one made by myself two years previously. It had a dirty blackish green tint, and was somewhat muddy, yet it answered perfectly well; but Dr. Loch is reported as having described a case in which alarming symptoms were caused by the use of an old solution. This may or may not have been the cause; but perhaps it will be better, until an improved method of keeping this solution be found out, to make a fresh solution every now and then, which can be done in a few seconds by putting one grain of the salt into 100 minims of water.

We may now, having discussed the use of apomorphine, enter into the question of the vomiting which is often stated to follow the use of hypodermic morphine. Some months ago, I saw in one of the journals—in the *Lancet*, I believe—a note saying that after a time solution of

morphine underwent a change, and that apomorphine was generated, and that, in consequence of the presence of apomorphine, such a solution would give rise to sickness. If such be the case, the vomiting is readily accounted for, and it would be our duty to avoid using old solutions of morphine. But is this so? The matter is one of extreme importance to us, and to our patients, and I would beg you to give it your careful consideration, and to express your opinion when I have concluded.

Morphine is, as you know, one of the remedies that lessens the irritability of the vomiting centres, and, like the generality of such remedies, it depresses the activity of the respiratory centre; hence morphine has been found a valuable medicine in vomiting of various forms. Yet it has also been freely credited with causing nausea and vomiting. That it does so occasionally is quite true, but that it does so often is, in my opinion, a fallacy.

I am now, of course, referring to the action of the pure morphine-salts. It does not follow, because sickness comes on immediately after a morphine-injection, that therefore the sickness is due simply to the morphine. We know that very slight causes will occasion faintness in some persons, and, similarly, that very slight exciting causes will give rise to vomiting in susceptible people. The prick of a hypodermic needle may occasion faintness and sickness, and so may the sight of one speck of blood at the site of a hypodermic injection. We must, therefore, take into account individual peculiarities, the state of the heart and the nervous system; and bear in mind that a drop of water subcutaneously injected may give rise, in some nervous persons, to very unpleasant symptoms.

But, though we may make due allowance for idiosyncrasy, we have still to account for the morphine-vomiting often alluded to by skilled observers. I would ask you to consider whether any one morphine-salt more than another predisposes to vomiting. Mr. Thomas, of Liverpool, in a paper published in the *Liverpool and Manchester Reports*, many years ago, claimed for sulphate of morphine that its use was never attended by sickness, and this statement has been corroborated.

To the best of my belief, other observers have claimed exemption for the neutral tartrate, and for the bimeconate of morphine, and I now claim a very considerable exemption for the pure acetate. In twenty years of hypodermic practice, I have noted that the occurrence of vomiting has been quite exceptional. I do not believe it has happened in more than about one per cent. of all my cases, and the only morphine-injection I have ever used has been the solution of the acetate, and that always made by myself.

When we speak of apomorphine, we mean the hydrochlorate of apomorphine, $C_{17}H_{17}NO_2HCl$, which is an artificial alkaloid made by heating morphine with concentrated hydrochloric acid.

It is quite certain, however long we keep our solutions of the sulphate, tartrate, bimeconate, or the acetate, that no chlorine can, by any possibility, be generated in them; therefore the formation of a hydrochlorate in them is impossible. But whether the base apomorphine ($C_{17}H_{17}NO_2$), which is simply morphine *minus* a molecule of water (H_2O), can be developed, in course of time, out of a solution of the four preceding salts in question, I can not answer with certainty in the negative; but it appears to me highly improbable that the base could thus be formed, because chemists, in order to obtain it, are obliged to treat the alkaloid with strong hydrochloric acid or a chloride.

So far, I have intentionally omitted all mention of the hydrochlorate of morphine. Let us now consider this salt.

In Lawson's work on *Sciatika*, he states that, in 5 per cent. of his cases, vomiting occurred, and he mentions that he always used the hydrochlorate. In this country, and up to a very recent time, the hydrochlorate was the salt generally used, but of late the acetate and

the sulphate have been gaining ground. In Germany, the hydrochlorate is still in pretty general use.

I cannot help thinking that vomiting has been more associated with the hydrochlorate than with the other morphine salts. If so, it may possibly be due to the gradual formation of apomorphine in old solutions of the hydrochlorate.

Those of you possessing old solutions of the hydrochlorate had better test them for apomorphine; and, meanwhile, I would recommend those who now use the hydrochlorate to give it up in favour of the acetate, which, without any doubt, is the very best morphine-salt we can use for hypodermic purposes.

Gentlemen, I thank you for the patience with which you have listened to my address. I have endeavoured to lay before you the chief points of interest in connection with the four most important of our hypodermic remedies.

I have made no attempt to enumerate all the painful troubles and complaints for which hypodermic injections of morphia can be used; but I trust I have succeeded in making clearer, than has hitherto been done, how and when morphine by itself, or atropine by itself, and atropine and morphine combined, can most advantageously be employed in the lessening of pain and the curing of disease.

You will probably agree with me that in many, if not in most cases, a local injection is better than a distant one; and I trust that the solutions which have been handed round to you, have made it very evident that there is no difficulty in making and keeping some hypodermic solutions. But I shall have failed in one of the chief objects of this address, if I have not succeeded in convincing you that there is need for increased caution in the administration of hypodermic injections, and need for greater judgment, care, and nicety in deciding upon the proper dosage for each individual patient.

DR. SPENDER (Bath), after thanking Dr. Jones for his exhaustive paper, alluded to the extreme desirability of letting the initial dose be very small, such as one-tenth of a grain for an adult man, and one-twelfth of a grain for an adult woman. Unless this precaution were observed, a misfortune, he said, would surely happen sooner or later. Moreover, an accident of this kind was ruinous in its consequences to a country practitioner; it was worse than a chloroform-accident, because there several persons shared the responsibility. It was, in Dr. Spender's opinion, always well to tell the patient, when administering morphine for the first time, not to expect much effect from the first dose. Should any effect be apparent, the patient had an unexpected pleasure, and the medical man was saved from the risk of untoward symptoms or a possible mishap. A long time since he had read of strong black coffee as being an excellent remedy to have by one when administering morphine; and now he always took care to have some strong hot coffee at hand whenever he had reason to think a mishap possible. The worst of these accidents was, he said, that they might happen with all the organs apparently in perfect condition, and with the individual in the best of health; and, therefore, they were apt to come without the slightest warning, and quite unexpectedly.

DR. SHEEN (Cardiff) said it was probably only too true that morphine was often given in doses far too large, and sometimes, possibly, with fatal results. There could be no doubt that morphine, when injected subcutaneously, was absorbed into the system, and did not act simply locally. He was glad to hear what Dr. Jones had said as to the greater stability of the stronger solutions; his own was 1 in 6.

MR. HANCOCKE WATHEN (Clifton) dwelt on the need for increased caution in the use of injections. He related circumstances in which morphine had been employed with culpable negligence.

The PRESIDENT (Professor Fraser) expressed the thanks of the meeting to Dr. Talfourd Jones, and regretted that time would not admit of a further and fuller discussion of so important a subject.

